Imcivree®
(setmelanotide)

FDA INDICATIONS AND USAGE[1]

IMCIVREE® is a melanocortin 4 (MC4) receptor agonist indicated to reduce excess body weight and maintain weight reduction long term in adults and pediatric patients 2 years of age and older with syndromic or monogenic obesity due to:

- Bardet-Biedel syndrome (BBS)
- Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

Limitations of Use:
IMCIVREE is not indicated for the treatment of patients with the following conditions as IMCIVREE would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign.
- Other types of obesity not related to BBS or POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

APPROVAL CRITERIA[1,2,3,4]

Obesity Due to Proopiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency

1. Patient meets FDA labeled age **AND**;
    a. Genetic testing demonstrates homozygous or compound heterozygous mutations in one of the following genes: POMC, PCSK1, or LEPR.
    b. The genetic variant is interpreted as pathogenic, likely pathogenic, or of uncertain significance.
    c. Patient is ≥ 18 years of age: Patient body mass index (BMI) ≥ 30 kg/m2 **OR** Patient is 6 to 17 years of age: Patient weight ≥ 95th percentile for age and sex **OR** Patient is 2 to 6 years of age: Patient weight ≥ 15kg and ≥ 97th percentile for age and sex **AND**;
2. Is being prescribed by or in consultation with an endocrinologist, a geneticist, or a physician who specializes in metabolic disorders **AND**;
3. The prescriber has documented the patients baseline weight and BMI **AND**;
4. The prescriber verifies the patient is not suicidal or have uncontrolled depression **AND**;
5. The prescriber has counselled the patient regarding potential sexual adverse reactions.

Bardet-Biedl Syndrome

1. Patient meets FDA labeled age **AND;**

2. Patient has the diagnosis of Bardet-Biedl Syndrome (BBS) **AND**;
3. Is being prescribed by or in consultation with an endocrinologist, a geneticist, or a physician who specializes in metabolic disorders **AND**;
4. Patient is ≥ 18 years of age: Patient currently has a body mass index (BMI) ≥ 30 kg/m2 **OR** Patient is 2 to 17 years of age: Patient weight ≥ 15kg and ≥ 97th percentile for age and sex **AND**;
5. The prescriber has documented the patients baseline weight and BMI **AND**;
6. The prescriber verifies the patient is not suicidal or have uncontrolled depression **AND**;
7. Prescriber has submitted chart notes which establish that other causes of obesity have been ruled out.

DENIAL CRITERIA [1]

1. Failure to meet approval criteria **OR**;
2. Patient has obesity due to suspected POMC-, PCSK1-, or LEPR-deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign **OR**;
3. Is being used for other types of obesity not related to POMC, PCSK1 or LEPR deficiency or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity **OR**;
4. Patient has moderate, severe, or end stage renal disease **OR**;
5. The patient is pregnant or breastfeeding.

CAUTIONS[1]

- Monitor for disturbances in sexual arousal.
- Patients should be monitored for depression and suicidal ideation.
- May cause generalized increased skin pigmentation and darkening of pre-existing nevi.
- Serious and fatal adverse reactions including “gasping syndrome” can occur in neonates and low birth weight infants treated with benzyl alcohol-preserved drugs.

DURATION OF APPROVAL

- Initial Approval: up to 3 months
- Reauthorization Approval: up to 12months if the prescriber documents the patient’s current weight or BMI and the patient has achieved weight loss ≥5% of the baseline body weight or ≥5% of BMI.

QUANTITY LIMIT

- 9ml per month

REFERENCES / FOOTNOTES:

1. Imcivree® subcutaneous injection [prescribing information]. Boston, MA: Rhythm Pharmaceuticals; March 2025.
2. Clément K, van den Akker E, Argente J, et al; setmelanotide POMC and LEPR Phase 3 Trial Investigators. Efficacy and safety of setmelanotide, an MC4R agonist, in individuals with severe obesity due to LEPR or POMC deficiency: single-arm, open-label, multicentre, phase 3 trials. Lancet Diabetes Endocrinol. 2020 Dec;8(12):960-970.
3. Poitou C, Mosbah H, Clément K. Mechanisms in endocrinology: update on treatments for patients with genetic obesity. Eur J Endocrinol. 2020 Nov;183(5):R149-R166.
4. Stijnen P, Ramos-Molina B, O'Rahilly S, et al. PCSK1 Mutations and Human Endocrinopathies: From Obesity to Gastrointestinal Disorders. Endocr Rev 2016; 37(4):347-71.